Remarks

New claims 87-90 are added for purposes of interference. Support for these claims can be found throughout the specification. Because applicant is suggesting an interference, applicant will discuss the specific support for the new claims in the claim chart provided below pursuant to 37 C.F.R. § 41.202(a)(5).

Applicant has cancelled previously pending claims 85-86 to expedite declaration of an interference. Applicant reserves the right to present claims to the cancelled subject matter in this or another application at a later date.

Applicant suggests an interference with US Patent No. 6,787,523 ("the '523 patent"). Applicant notes that the Board has made it quite clear that interferences exist for the limited purpose of determining priority between a patentee (or an applicant) and an applicant. MPEP § 2301. While an interference may determine that an involved patent is not valid, 35 U.S.C. § 135(a), interferences are not "generalize patent cancellation proceedings." Final Rule, 69 Fed. Reg. 49960 (August 12, 2004) at p. 49991, col. 2. Rather, the "purpose of the interference is to resolve priority between the patentee and the applicant so that an examiner can determine whether the applicant is entitled to a patent." *Dietz-Band v. Gray*, 73 USPQ2d 1857, 1859 (Bd. Pat. App. & Int. 2004)(nonprecedential).

That is the purpose of the present suggestion. In the Office Action mailed February 24, 2004, the Examiner rejected the claims over the published PCT application counterpart of the '523 patent, which had not yet issued. [Office Action of February 24, 2004 at p. 5.] Applicant responded by filing a Declaration under 37 C.F.R. § 1.131, antedating the published PCT application as a reference under 35 U.S.C. § 102(a). In response, the Examiner withdrew the rejection because a § 131 declaration can remove a § 102(a) reference. But the '523 patent issued in the interim, so the Examiner rejected the claims under 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a) over the '523 patent.[1] A § 131 declaration can remove a US patent as a § 102(e) reference if the patent does not claim the same patentable invention. But, if the US patent claims the same patentable invention, the § 131 declaration is ineffective. MPEP § 715 II (B) at p. 700-271, col. 2. Because the Examiner accepted the § 131 declaration as removing the published

PCT application but not the corresponding '523 patent, the Examiner necessarily found that the '523 patent claimed the same patentable invention.

When a US patent claims the same patentable invention as an applicant, the patent "can then be overcome only by way of an interference." MPEP § 715.05 at p. 700-279, col. 2. Accordingly, applicant is suggesting an interference with the '523 patent.

"Since 37 CFR 1.131 defines 'same patentable invention' in the same way as the interference rules (37 CFR 41.203(a)), the USPTO cannot prevent an applicant from overcoming a reference by a 37 CFR 1.131 affidavit or declaration on the grounds that the reference claims applicant's invention and, at the same time, deny applicant an interference on the grounds that the claims of the application and those of the reference are not for substantially the same invention." MPEP § 715.05 at p. 700-278, col. 2. Accordingly, an interference should be declared to allow applicant to obtain a determination from the PTO as to whether applicant is entitled to a patent.

Applicant will address each of the requirements for suggesting an interference in the order set forth in 37 C.F.R. § 41.202(a).

§ 41.202(a)(1)

Applicant seeks an interference with U.S. Patent No. 6,787,523 ("the '523 patent"), which issued on September 7, 2004.

§ 41.202(a)(2)

Applicant believes all the claims of the '523 patent (claims 1-24) interfere with all the pending claims in the present application (claims 87-90).

Applicant proposes one count:

Count 1

the method of claim 87 of the present application.

or

the method of claim 1 of the '523 patent.

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[1] The Examiner noted that at least 5 other related patents issued the same day as the '523 patent but relied upon just the '523 patent as representative of the others because it issued from an parent application of the others. [Office Action of December 1, 2004 at p. 3.]

Claim 87 of the present application and claim 1 of the '523 patent are identical. Similarly, claims 88-90 of the present application are identical to claims 2, 3, and 14, respectively, of the '523 patent. Those are the only claims of the present application.

The '523 patent also contains independent claims 8 and 22. Those claims differ from claim 1 merely by having the additional limitations of a standard dosage and monitoring the immune response by detecting the antibodies it generates. Neither of those previously known elements are patentable distinctions from the proposed count.

The '523 patent contains additional dependent claims 4-7, 9-13, 15-16, 18-21, and 23-24. Similar to independent claim 8 of the '523 patent, claims 9, 20, and 24 recite standard dosages. Similar to independent claim 22 of the '523 patent, claim 13 recites monitoring the immune response. Similar to claim 14 of the '523 patent, claims 15, 16, and 21 recite standard timings for adjuvant administration.

Claims 17-19, 21[2], and 23 recite standard adjuvants known in the prior art. Claims 4-7 of the '523 patent relate to the patient's risk of Alzheimer's disease, factors known in the prior art. Claim 10 recites a standard form of Aβ peptide to be administered, and claims 11-12 recite standard routes for administering an immunogenic composition.

Thus, all the claims of the '523 patent other than independent claim 1 differ from claim 1 merely by reciting standard elements known in the prior art. Accordingly, none of the claims of the '523 patent are patentably distinct from claim 1 of the '523 patent; that is, count 1.

Similarly, all the claims of the present application other than independent claim 87 differ from claim 87 merely by reciting standard elements known in the prior art. Accordingly, none of the claims of the present application are patentably distinct from claim 87 of the present application; that is, count 1. Thus, claims 87-90 of the present application and claim 1-24 of the '523 patent correspond to count 1.

For the Examiner's convenience, Applicants file herewith a suggested Interference Initial Memorandum (Form PTO-850) setting forth this information for count 1.

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[2] Dependent claim 21 adds standard limitations for both the timing of the adjuvant administration and the identity of the adjuvant.

§ 41.202(a)(3)

The following claim chart compares the independent claims of the two parties recited in the count. Because the claims are identical, they interfere within the meaning of § 41.203(a).

Count 1

Claim 87 filed herewith	Claim 1 of US 6,787,523 B1
A method of preventing or treating a disease characterized by an amyloid deposit of Aβ in a patient, comprising:	A method of preventing or treating a disease characterized by an amyloid deposit of Aβ in a patient, comprising:
administering an Aβ peptide and an adjuvant in a regime effective to induce an immune response comprising antibodies to the Aβ peptide,	administering an Aβ peptide and an adjuvant in a regime effective to induce an immune response comprising antibodies to the Aβ peptide,
the adjuvant enhancing the immune response to the Aβ peptide,	the adjuvant enhancing the immune response to the Aβ peptide,
and thereby prevent or treat the disease in the patient.	and thereby prevent or treat the disease in the patient.

§ 41.202(a)(4)

The present application was filed on November 6, 2001, and claims priority to application Serial No. 09/594,366, filed June 15, 2000, and provisional application 60/139,408, filed June 16, 1999. Applicant has shown that claims 87-90 are entitled to benefit of that filing date of June 16, 1999.

The '523 patent issued from application Serial No. 09/201,43, filed on November 30, 1998, and claims priority to provisional applications 60/080,970, filed April 7, 1998, and 60/067,740, filed December 2, 1997.

Because the '523 patent claims priority to the earlier date of December 2, 1997, applicant must show that it could establish an invention date before December 2, 1997 to provoke an interference. *See* 37 C.F.R. § 41.202(d)(1). To do so, applicant must show an earlier conception and reasonable diligence from before December 2, 1997 to its benefit date of June 16, 1999.

The Paulus Declaration and the attached affidavits of Vladamir Volloch and Henry Paulus corroborate an earlier conception date. [Paulus Dec. at ¶ 3.] Thus, applicant must show reasonable diligence from before December 2, 1997 to its benefit date of June 16, 1999.

Applicant recognizes that this is a larger period for reasonable diligence than is often proven. However, this case presents the very situation that continues to compel the United States to resist pressure to abandon its first-to-invent system in favor of the first-to-file system used by the rest of the world: allowing individual (or institutional) applicants with few resources to compete with large corporations that have the resources to win a race to the PTO.

The law has long and consistently recognized that such inventors or institutions can satisfy the reasonable diligence requirement by attempting to raise funds to reduce the invention to practice. *See, e.g., Marconi Wireless Co. v. U.S.*, 320 US 1, 34 (1943)(finding diligence of seven months because applicant "was diligent in obtaining capital to promote his invention."); *Christensen v. Ellis*, 17 App. DC 498, 501-02 (DC Cir. 1901)(delay in actual reduction to practice excused or amounted to diligence because inventor "was without means and was compelled to seek aid for the exploitation of his ideas."); *Wayne v. Tew*, 290 F. 311, 313-14 (DC Cir. 1923)(Six-month delay in constructively reducing invention to practice constituted diligence because inventor with no other means of support was attempting to raise funds to reduce invention to practice); *American Standard, Inc. v. Pfizer Inc.*, 14 USPQ2d 1673, 1649 (D. Del. 1989)(finding diligence of 11 months based upon attempts to obtain funding to reduce invention

to practice and conducting experiments to support the fundraising); *Hybritech Inc. v. Abbott Labs.*, 4 USPQ2d 1001, 1006 (C.D. Cal. 1987) (finding reasonable diligence of 16 months based on, *inter alia,* need for a startup company to get financing), *aff'd,* 849 F.2d 1446 (Fed. Cir. 1988); *see also* Revise and Caesar, *Interference Law and Practice* § 191 ("[C]onsideration must be given to the situation of the inventor, including his state of health, financial condition, skill and available time.").

As discussed below, Applicant spent all his time during the critical period attempting to raise funds to reduce his invention to practice and, in the process, to support himself and his family. Those facts are established in declarations and supporting documents from seven different witnesses, including 6 corroborating witnesses who are not inventors. For purposes of establishing priority under 41 C.F.R. § 202(d)(1), the statements in these declarations must be accepted as true. *See Basmadjian v. Landry,* 54 USPQ2d 1617, 1624-26 (Bd. Pat. App. & Int. 1997). Because applicant provides evidence of sufficient facts to establish reasonable diligence, Applicant establishes reasonable diligence sufficient for declaring an interference.

Applicant's activities before December 2, 1997

Before December 2, 1997, applicant had moved well-beyond conception and toward a reduction to practice. As shown in the NIH Grant Application applicant filed October 21, 1997, applicant had already synthesized numerous Aβ peptides, including full-length, truncated, and transition state analogs. [B000243-244.] Those antibodies had the ability to solubilize aggregates of Aβ peptides. [B000255.]

Applicant had also immunized normal mice with these peptides (in an adjuvant). [B000247.] Applicant had obtained antibodies from those mice and confirmed that they bound Aβ peptide *in vitro*. [B00248-49.] Applicant had produced monoclonal antibodies with these mice and confirmed that they also bound Aβ peptide *in vitro*. [B000248-49; B000250-52.]

Applicant had also extended those studies to *in vivo* mice. Applicant had demonstrated that the monoclonal antibodies to Aβ peptide bound Aβ peptide in normal mice. [B000253.] Applicant had also demonstrated that the monoclonal antibodies caused Aβ peptide administered to the mice to be retained in the circulation rather than crossing into the brain, where they could aggregate into an amyloid deposit. [B000253-254.] Applicant also showed that the brains of

those mice exhibited an amorphous distribution of Aβ peptide, as would be expected for low levels of Aβ peptide in brain free of amyloid plaques. B00254.]

Finally, Applicant had obtained Alzheimer's model transgenic mice. [B000254-56; B000258.] Applicant has started the long and difficult process of using those mice to develop a colony of sufficient size for experiments. [B000258.] Applicant had also planned numerous experiments whose results would take at least almost 1 year from inception, which was the time it would take for the model mice to exhibit Alzheimer's symptoms. [B000254.]

Applicant's Scientific Diligence

The reason this work appears in a NIH grant application is that applicant had no means to support his research, nor his family, at that time. Applicant was a Senior Scientist at the Boston Biomedical Research Institute (BBRI). [Raso Decl. at ¶ 1; Kaye Dec. at ¶ 3.] BBRI supports itself, and its faculty members, on federal grants. [Raso Dec at ¶ 2; Morgan Decl. at ¶ 3-9; Paulus Dec. at ¶ 4-6; Kaye Dec. at ¶¶ 2-4.] Applicant had run out of funding as of September 15, 1997. [Raso Dec. at ¶ 13; Morgan Decl. at ¶ 15; Paulus Dec. at ¶¶ 8-9; Kaye Dec. at ¶¶ 7-10, 12.] While applicant continued to hold a position at BBRI, he had no source of income, and he was in serious jeopardy of losing his faculty position at BBRI, as well as his remaining lab space. [Raso Dec. at ¶¶ 2-13; Morgan Decl. at ¶¶ 9-17; Paulus Dec. at ¶¶ 10-11; Kaye Dec. at ¶¶ 10-11.] Applicant had lost his source of income, and was facing losing his appointment and his remaining laboratory space all because he did not have a source of funding. [Raso Dec. at ¶¶ 12-14; Morgan Decl. at ¶ 14-17; Paulus Dec. at ¶¶ 10-11; Kaye Dec. at ¶¶ 13-15.]

Seeking to reduce his invention to practice, to obtain a source of income, and to retain his position at BBRI, applicant was constantly working on grant applications in 1997-1999. [Raso Dec. at ¶ 17; Paulus Dec. at ¶¶ 12-13; Kaye Dec. at ¶¶ 16; Bourgeois Dec. at ¶ 5.] Applicant worked many nights and weekends to obtain the data and write these grant applications. [Raso Dec. at ¶ 18; Bourgeois Dec. at ¶ 6.] As can be seen from the chart in his declaration, these grant applications all concerned treating or preventing Alzheimer's Disease by Aβ peptide immunotherapy. [Raso Dec. at ¶ 17; Paulus Dec. at ¶ 13; Kaye Dec. at ¶ 16; Bourgeois Dec. at ¶ 6.] Applicant filed 12 such applications from December 2, 1997 until June 16, 1999. [Raso Dec. at ¶ 17; Paulus Dec. at ¶ 12; Kaye Dec. at ¶ 16.] This is an exceptional number, and resulted

from applicant "desperately trying" to save his career and continue his research. [Raso Dec. at ¶ 18; Paulus Dec. at ¶ 13; Kaye Dec. at ¶ 16.]

Because applicant's desperate efforts were focused on obtaining funding, he did not maintain the most detailed notes about his experiments. [Raso Dec. at ¶ 18; Bourgeois Dec. at ¶ 7.] He only maintained notes that he deemed sufficient to enable him to prepare the grant applications and, hopefully, obtain funding to further his research. [Raso Dec. at ¶ 18; Bourgeois Dec. at ¶ 7.] Nonetheless, applicant has submitted [Raso Dec. at ¶ 20; Ex. O; Bourgeois Dec. at ¶ 8, Ex. B] and discussed many of these documents. [Raso Dec. at ¶¶ 20-86; Bourgeois Dec. at ¶¶ 9-44.] In addition, applicant has submitted a chart summarizing those documents. [Raso Dec. at ¶ 20, Ex. O; Bourgeois Dec. at ¶ 8, Ex. A.]

Attorney Diligence

Applicant first submitted invention disclosures for his method of treating or preventing Alzheimer's Disease on November 22, 1996, November 4, 1997, and December 7, 1998. [Raso Dec. at ¶ 90.] BBRI decided to prepare and file a patent application in response to the 1998 invention disclosure. [Raso Dec. at ¶ 90.] BBRI's outside consultant patent agent contacted BBRI's outside patent attorney shortly before January 27, 1999 and sent a disclosure to him on January 27, 1999. [Farrell Dec. at ¶ 4.] BBRI's outside patent attorney received the disclosure on February 1, 1999, and he studied it that day. [Farrell Dec. at ¶ 5.]

BBRI's outside patent attorney assigned the application to a full-time technical specialist, the technical specialist studied the disclosure on February 5, 1999 and prepared a memorandum about it on February 8, 1999. [Farrell Dec. at ¶ 6.]. The technical specialist and applicant spoke and corresponded about the declaration several times her in February and March 1999. [Raso Dec. at ¶ 9; [Farrell Dec. at ¶¶ 7-14.] After several drafts were exchanged, the provisional application was filed on June 16, 1998. [Raso Dec. at ¶ 92; Farrell Dec. at ¶ 17.] Specifically, the technical specialist and/or the outside patent attorney worked on the application on February 23, February 26, March 1, March 2, March 4, March 5, March 8, March 9, March 10, March 17, March 18, March 19, March 22, March 23, March 24, March 25, March 29, March 31, April 15, April 19, April 22, May 4, May 13, May 20, May 21, May 25, June 14, and June 16. [Farrell Dec. at ¶¶ 7-17.]

The technical specialist took up the application in its chronological order. [Farrell Dec. at ¶ 18.] The technical specialist did not give preference to other work unless it came chronologically earlier or was subject to earlier deadlines established by the PTO or statute. [Farrell Dec. at ¶ 18.]

Applicant has established reasonable diligence

Section 102(g) requires only "*reasonable* diligence." (Emphasis added). Reasonable diligence is not subject to "the legal rigor of conception and reduction to practice." *Brown v. Barbacid*, 436 F.3d 1376, 1380 (Fed. Cir. 2006). Thus, it may be shown by a variety of activities, as precedent illustrates. *Id.*

Such precedent of over 100 years, *e.g., Christensen*, 17 App. DC at 501-02, including from the Supreme Court, *Marconi,* 320 US at 34, has consistently held that an inventor's attempts to raise funds to reduce the inventor's invention to practice must be considered in the diligence analysis and can satisfy the reasonable diligence requirement. The *American Standard* case is particularly instructive. There, the inventors spent 11 months seeking funding and designing experiments for purposes of raising those funds and reducing the invention to practice. 14 USPQ2d at 1649. Because the inventors were attempting to reduce the invention to practice, and fundraising attempts to achieve that goal may be considered, the court found that the inventors had established reasonable diligence. *Id.*

As in *American Standard*, applicant spent all his time during the critical period seeking funding and designing experiments for purposes of raising those funds and reducing the invention to practice. Because applicant was attempting to reduce the invention to practice, and applicant's fundraising attempts to achieve that goal may be considered, applicant has established reasonable diligence.

Moreover, attorney diligence can be tacked onto and/or can supplement scientific diligence. *See Bey v. Kollonitsch*, 806 F.2d 1024 (Fed. Cir. 1986). Combining the attorney diligence beginning on December 7, 1998 with the scientific diligence beginning before December 2, 1997, further strengthens applicant showing of diligence.

§ 41.202(a)(5)

The following charts of the claims filed herewith show the written description of each new claim in applicant's specification.

New Claim	Support in Specification
87. A method of preventing or treating a disease characterized by an amyloid deposit of Aβ in a patient, comprising:	18. A method for reducing levels of β-amyloid in the brain of an animal, comprising the steps: . . . . [p. 63] 23. A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps . . . . [p. 64] Therapeutic applications of this method include treating patients diagnosed with, or at risk for Alzheimer's disease. [p. 4, lines 22-24] Therefore, the above techniques are useful for preventing the formation of amyloid plaques in the brain of an animal. This is especially applicable to an animal which is considered at risk for the development of amyloid plaques; a risk which may result from a genetic predisposition or from environmental factors. Administration of antibodies, or immunization of the animal to produce endogenous antibodies, to β-amyloid can be of therapeutic benefit to such an animal (e.g., a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease). [p. 11, lines 2-12]
administering an Aβ peptide and an adjuvant in a regime effective to induce an immune response comprising antibodies to the Aβ peptide,	18. A method for reducing levels of β-amyloid in the brain of an animal, comprising the steps: a) providing an antigen comprised of an epitope which is present on β-amyloid endogenous to the animal; and b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β-amyloid. [p. 63]

	23. A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps: a) providing an antigen comprised of an epitope which is present on β-amyloid endogenous to the animal; and b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β-amyloid. [p. 64] <u>Antibodies Elicited With the β-Amyloid Vaccines</u> Normal BALB/c mice were immunized by standard procedures with the KLH-linked Aβ vaccines described above. * * * Sera and monoclonal antibodies obtained were characterized for binding to Aβ. Table 1 shows the results from an ELISA run with 1/100 diluted serum from two non-immunized control mice versus {fraction (1/100)} and {fraction (1/1000)} diluted serum from a mouse that was immunized with a central region Aβ peptide-KLH vaccine. The free Aβ peptide was adsorbed directly onto the microtitre plate to avoid detection of anti-KLH antibodies in the serum. Table 1 ELISA for Binding to the Central Region Aβ Peptide [p. 24, line 27, through p. 25, line 8] Results presented in Table 2 indicate that the antibodies generated to the peptide fragments also bound full length $A\beta_{1-43}$. [p. 25, lines 24-26] The results indicate that mice immunized with the cocktail of the three peptide antigens produced serum containing antibodies which react with the amino-terminal, central region, and carboxyl-terminal peptides, as well as with the full-length Aβ 40-mer and 43-mer. [p. 29,

	lines 16-21] Vaccine Trials in Non-human Primates Given the potential importance of β-amyloid vaccine therapy for human patients of Alzheimer's disease, a human-compatible, alum-based Aβ peptide vaccine preparation has been tested in non-human primates. Antibody production and safety studies for the human-compatible β-amyloid vaccines have commenced in Cynomolgus monkeys (*Macaca fascicularis*). This animal system is highly relevant to human applications since the predicted amino acid sequence of β-amyloid in these primates is identical to humans, and their basic physiology and immunological systems closely approximate those which will be encountered in a clinical situation. * * * The Cynomolgus monkeys mounted a strong immune response to a single injection of the simplest vaccine preparation composed of the full length β-amyloid peptide adsorbed to an aluminum hydroxide gel. The specificity of those early anti-β-amyloid antibodies was characterized by ELISA using various Aβ peptide fragments (Table 6). This analysis indicated that the monkeys produced antibodies that bind to the full-length peptide and react with its amino-terminal, central and carboxyl-terminal regions. [p. 30, lines 1-32] Briefly, mice were injected i.p. with antigen emulsified in complete Freunds adjuvant, followed by a second course in incomplete Freunds adjuvant. [p. 34, lines 12-14]
the adjuvant enhancing the immune response to the Aβ peptide,	These represent powerful delivery systems for β-amyloid peptides, and are known to induce an excellent, high titer immune response when used with alum as an adjuvant. [p. 32, lines 10-12] The produced fusions will be used with an

	aluminum hydroxide gel adjuvant to generate potent vaccines. [p. 32, lines 19-21] Briefly, mice were injected i.p. with antigen emulsified in complete Freunds adjuvant, followed by a second course in incomplete Freunds adjuvant. [p. 34, lines 12-14]
and thereby prevent or treat the disease in the patient.	Therapeutic applications of this method include treating patients diagnosed with, or at risk for Alzheimer's disease. [p. 4, lines 22-24] Therefore, the above techniques are useful for preventing the formation of amyloid plaques in the brain of an animal. This is especially applicable to an animal which is considered at risk for the development of amyloid plaques; a risk which may result from a genetic predisposition or from environmental factors. Administration of antibodies, or immunization of the animal to produce endogenous antibodies, to β-amyloid can be of therapeutic benefit to such an animal (e.g., a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease). [p. 11, lines 2-12]
88. The method of claim 87, wherein the patient is a human.	Therapeutic applications of this method include treating patients diagnosed with, or at risk for Alzheimer's disease. [p. 4, lines 22-24] Therefore, the above techniques are useful for preventing the formation of amyloid plaques in the brain of an animal. This is especially applicable to an animal which is considered at risk for the development of amyloid plaques; a risk which may result from a genetic predisposition or from environmental factors. Administration of antibodies, or immunization of the animal to produce endogenous antibodies, to β-amyloid can be of therapeutic benefit to such an animal (e.g., a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease). [p. 11, lines 2-12]

	Vaccine Trials in Non-human Primates Given the potential importance of β-amyloid vaccine therapy for human patients of Alzheimer's disease, a human-compatible, alum-based Aβ peptide vaccine preparation has been tested in non-human primates. Antibody production and safety studies for the human-compatible β-amyloid vaccines have commenced in Cynomolgus monkeys (*Macaca fascicularis*). This animal system is highly relevant to human applications since the predicted amino acid sequence of β-amyloid in these primates is identical to humans, and their basic physiology and immunological systems closely approximate those which will be encountered in a clinical situation. * * * The Cynomolgus monkeys mounted a strong immune response to a single injection of the simplest vaccine preparation composed of the full length β-amyloid peptide adsorbed to an aluminum hydroxide gel. The specificity of those early anti-β-amyloid antibodies was characterized by ELISA using various Aβ peptide fragments (Table 6). This analysis indicated that the monkeys produced antibodies that bind to the full-length peptide and react with its amino-terminal, central and carboxyl-terminal regions. [p. 30, lines 1-32] An "immune system deficiency" shall mean a disease or disorder in which the subject's immune system is not functioning in normal capacity or in which it would be useful to boost a subject's immune response for example to eliminate a tumor or cancer . . . or a viral . . . , fungal . . . , bacterial or parasitic . . . infection in a subject. [Page 11, lines 21-26.] Based on their immunostimulatory properties, oligonucleotides containing at least one unmethylated CpG dinucleotide can be administered to a subject in vivo to treat an "immune system deficiency". Alternatively, oligonucleotides containing at least one

	unmethylated CpG dinucleotide can be contacted with lymphocytes (e.g. B cells or NK cells) obtained from a subject having an immune system deficiency ex vivo and activated lymphocytes can then be reimplanted in the subject. [Page 21, lines 11-16.]
89. The method of claim 87, wherein the disease is Alzheimer's disease.	Therapeutic applications of this method include treating patients diagnosed with, or at risk for Alzheimer's disease. [p. 4, lines 22-24] Therefore, the above techniques are useful for preventing the formation of amyloid plaques in the brain of an animal. This is especially applicable to an animal which is considered at risk for the development of amyloid plaques; a risk which may result from a genetic predisposition or from environmental factors. Administration of antibodies, or immunization of the animal to produce endogenous antibodies, to β-amyloid can be of therapeutic benefit to such an animal (e.g., a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease). [p. 11, lines 2-12] Vaccine Trials in Non-human Primates Given the potential importance of β-amyloid vaccine therapy for human patients of Alzheimer's disease, a human-compatible, alum-based Aβ peptide vaccine preparation has been tested in non-human primates. Antibody production and safety studies for the human-compatible β-amyloid vaccines have commenced in Cynomolgus monkeys (*Macaca fascicularis*). This animal system is highly relevant to human applications since the predicted amino acid sequence of β-amyloid in these primates is identical to humans, and their basic physiology and immunological systems closely approximate those which will be encountered in a clinical situation. * * * The Cynomolgus monkeys mounted a strong

	immune response to a single injection of the simplest vaccine preparation composed of the full length β-amyloid peptide adsorbed to an aluminum hydroxide gel. The specificity of those early anti-β-amyloid antibodies was characterized by ELISA using various Aβ peptide fragments (Table 6). This analysis indicated that the monkeys produced antibodies that bind to the full-length peptide and react with its amino-terminal, central and carboxyl-terminal regions. [p. 30, lines 1-32]
90. The method of claim 87, wherein the adjuvant and the Aβ peptide are administered together as a composition.	Vaccine Trials in Non-human Primates Given the potential importance of β-amyloid vaccine therapy for human patients of Alzheimer's disease, a human-compatible, alum-based Aβ peptide vaccine preparation has been tested in non-human primates. Antibody production and safety studies for the human-compatible β-amyloid vaccines have commenced in Cynomolgus monkeys (*Macaca fascicularis*). This animal system is highly relevant to human applications since the predicted amino acid sequence of β-amyloid in these primates is identical to humans, and their basic physiology and immunological systems closely approximate those which will be encountered in a clinical situation. * * * The Cynomolgus monkeys mounted a strong immune response to a single injection of the simplest vaccine preparation composed of the full length β-amyloid peptide adsorbed to an aluminum hydroxide gel. The specificity of those early anti-β-amyloid antibodies was characterized by ELISA using various Aβ peptide fragments (Table 6). This analysis indicated that the monkeys produced antibodies that bind to the full-length peptide and react with its amino-terminal, central and carboxyl-terminal regions. [p. 30, lines 1-32]

§ 41.202(a)(6)

The following chart shows that claim 87 is supported by application Serial No. 60/139,408, filed June 16, 1999, entitling applicant to benefit of its filing date:

New Claim	Support in Serial No. 60/139,408
87. A method of preventing or treating a disease characterized by an amyloid deposit of Aβ in a patient, comprising:	18. A method for reducing levels of β-amyloid in the brain of an animal, comprising the steps: . . . . [p. 57] 23. A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps . . . . [p. 58] Therapeutic applications of this method include treating patients diagnosed with, or at risk for Alzheimer's disease. [p. 4, lines 22-24] Therefore, the above techniques are useful for preventing the formation of amyloid plaques in the brain of an animal. This is especially applicable to an animal which is considered at risk for the development of amyloid plaques; a risk which may result from a genetic predisposition or from environmental factors. Administration of antibodies, or immunization of the animal to produce endogenous antibodies, to β-amyloid can be of therapeutic benefit to such an animal (e.g., a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease). [p. 11, lines 2-12]
administering an Aβ peptide and an adjuvant in a regime effective to induce an immune response comprising antibodies to the Aβ peptide,	18. A method for reducing levels of β-amyloid in the brain of an animal, comprising the steps: a) providing an antigen comprised of an epitope which is present on β-amyloid endogenous to the animal; and b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β-amyloid. [p. 57] 23. A method for preventing the formation of

	amyloid plaques in the brain of an animal, comprising the steps: a) providing an antigen comprised of an epitope which is present on β-amyloid endogenous to the animal; and b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous β-amyloid. [p. 58] <u>Antibodies Elicited With the β-Amyloid Vaccines</u> Normal BALB/c mice were immunized by standard procedures with the KLH-linked Aβ vaccines described above. * * * Sera and monoclonal antibodies obtained were characterized for binding to Aβ. Table 1 shows the results from an ELISA run with 1/100 diluted serum from two non-immunized control mice versus {fraction (1/100)} and {fraction (1/1000)} diluted serum from a mouse that was immunized with a central region Aβ peptide-KLH vaccine. The free Aβ peptide was adsorbed directly onto the microtitre plate to avoid detection of anti-KLH antibodies in the serum. Table 1 ELISA for Binding to the Central Region Aβ Peptide [p. 22, line 18, through p. 25, line 1] Results presented in Table 2 indicate that the antibodies generated to the peptide fragments also bound full length $A\beta_{1-43}$. [p. 25, lines 14-16]
the adjuvant enhancing the immune response to the Aβ peptide,	These represent powerful delivery systems for β-amyloid peptides, and are known to induce an excellent, high titer immune response when used with alum as an adjuvant. [p. 32, lines 10-12] The produced fusions will be used with an

	aluminum hydroxide gel adjuvant to generate potent vaccines. [p. 32, lines 19-21] Briefly, mice were injected i.p. with antigen emulsified in complete Freunds adjuvant, followed by a second course in incomplete Freunds adjuvant. [p. 30, lines 8-10]
and thereby prevent or treat the disease in the patient.	Therapeutic applications of this method include treating patients diagnosed with, or at risk for Alzheimer's disease. [p. 4, lines 22-24] Therefore, the above techniques are useful for preventing the formation of amyloid plaques in the brain of an animal. This is especially applicable to an animal which is considered at risk for the development of amyloid plaques; a risk which may result from a genetic predisposition or from environmental factors. Administration of antibodies, or immunization of the animal to produce endogenous antibodies, to β-amyloid can be of therapeutic benefit to such an animal (e.g., a human who has a family history of Alzheimer's disease, or who is diagnosed with the disease). [p. 11, lines 2-12]

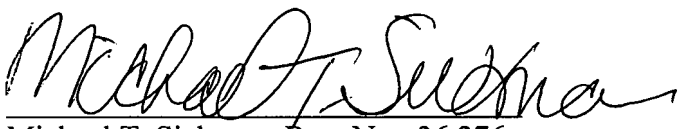
Consolidation of Prosecution

Applicant respectfully requests that any and all related applications of the parties be consolidated with the same examiner. *See* MPEP § 2304.01(b)("Ordinarily applications that are believed to interfere should be assigned to the same examiner."). This will ensure that the PTO takes uniform positions regarding applications to the same subject matter. *See* MPEP § 2304.01(b)("In an effort to maximize uniformity, when an examiner first becomes aware that a potential interference exists or any other interference issue arises during prosecution of an application, the examiner should bring the matter to the attention of an IPS in the examiner's TC.").

Conclusion

If the Examiner and/or the Interference Practice Specialist have any questions regarding this paper, they are invited to contact the undersigned to expedite declaration of an interference.

Respectfully submitted,



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